

**Remarks/Arguments**

Claims 21-37 remain in the application. Claims 21-37 are rejected.

Applicant notes that an acknowledgement has not been made of a claim for domestic priority under 35 U.S.C. 119(e). The Applicant has amended the application to include a paragraph perfecting priority under 35 U.S.C. 119(e) and making a specific reference to the prior U.S. Provisional Application No. 60/095,481. This information was included on the declaration at the time of entering the national phase.

Applicant further notes that an acknowledgement has not been made of a claim for domestic priority under 35 U.S.C. 120. The Applicant has amended the application to include a paragraph perfecting priority under 35 U.S.C. 120 and making a specific reference to the prior U.S. Patent Application No. 09/321,820 now issued as U.S. Patent No. 6,504,149. This information was included on the declaration at the time of entering the national phase.

Claims 21, 30, and 37 have been amended in order to avoid invoking 35 U.S.C. 112, sixth paragraph. In particular, all instances of phrases such as --the steps of--, and --step e) of--, etc. have been deleted. Applicant wishes to note for the record that the amendments are neither narrowing, nor are the amendments being made for a reason substantially related to patentability. Applicant respectfully submits that no new matter has been added in the amendments. Applicant further submits that claims 21, 30 and 37 are in allowable form, and favorable reconsideration is kindly requested.

**Claim Rejections under 35 U.S.C. § 103**

Claims 21, 22, 24, 25, 27, 29-31, 33, 34, 36, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buryakov et al. ("A new method of separation of multi-atomic ions by mobility at atmospheric pressure using a high-frequency amplitude-asymmetric strong electric field", International Journal Mass Spectrometry and Ion Processes, 1999).

Applicant disagrees with the statement at Page 3, line 3 of the Official Action mailed on October 7, 2003, and respectfully submits that the method used by Buryakov et al. is not “also suitable for isotope identification.” In particular, Buryakov et al. do not teach “identifying peaks in said compensation voltage scan **corresponding to said isotopes**” and “setting said direct current compensation voltage to correspond to one of said peaks, **so as to separate and enrich one of said two isotopes**,” as is claimed at claim 21. In fact, Buryakov et al. merely teach “identifying peaks in said compensation voltage scan” and “setting said direct current compensation voltage to correspond to one of said peaks so as to separate and enrich a desired ion” (see Official Action mailed on October 7, 2003, page 2, second last line to page 3, line 1).

Of course, many different types of ions are known. For example, two ions may be related one to the other as structural isomers (for instance leucine ions and isoleucine ions), as conformers (for instance protein ions that are folded into different 3-dimensional shapes), as isotopes of a same chemical element (for instance  $^{35}\text{Cl}^-$  and  $^{37}\text{Cl}^-$ ), etc. In general, a given method of separating and/or enriching one of the above-mentioned types of ions does not necessarily work for every other one of the above-mentioned types of ions. As an example, gas chromatography (GC) and High Performance Liquid Chromatography (HPLC) are used routinely to separate mixtures of different structural isomers, but are incapable of separating mixtures of different isotopes of a same chemical element or mixtures including compounds of differing isotopic composition. Mass spectrometry, on the other hand, is capable of differentiating between ions of different isotopes of a same chemical element or between ions of differing isotopic composition (albeit under high vacuum conditions), but generally cannot differentiate between different structural isomers or between different conformers. As such, based solely upon the teaching of Buryakov et al. that FAIMS can separate ions **in general**, one of ordinary skill in the art at the time of the invention could not have reasonably predicted that ions of different isotopes of a same chemical element or ions of differing isotopic composition could also be separated and/or enriched using FAIMS. Accordingly, the method that is used by Buryakov et al. **cannot** “also be suitable for isotope identification” absent

specific teaching that is directed to identifying and separating ions of different isotopes or ions of differing isotopic composition.

Applicant respectfully traverses the rejection of claim 21 under 35 U.S.C. 103(a) as being unpatentable over Buryakov et al. In particular, Applicant submits that the modification as proposed at Page 3, lines 3-7 of the Official Action mailed on October 7, 2003, is unmotivated. The rational that is provided for making the modification is that “the prior art state that it provides an improved method of ion separation even for ions with similar masses (page 145, col. 2, last paragraph) and for homologous ions (page 148, Conclusion).” In fact, at page 145, col. 2, last paragraph Buryakov et al. actually states “Ions of diverse types differ markedly in mobility even if they have similar masses. . . . Differing in masses only by 2u these ions have marked differences in  $E_c$ , **which can be connected with the differences in their spatial structure.**” Buryakov et al. clearly teach at page 145, col. 2, last paragraph that separation, in terms of  $E_c$  (compensation voltage), of the ions with similar masses can be connected with the differences in their **spatial structure**. Applicant respectfully submits that rather than suggesting the proposed modification to one of ordinary skill in the art at the time the invention was made, the statement at page 145, col. 2, last paragraph actually teaches away from making the proposed modification. In particular, at page 5, lines 10 to 13 of the international publication, the term “isotopes” is defined as “members of a chemical-element family that have two or more nuclides with the same number of protons but different numbers of neutrons, such that they differ in atomic mass but have the same chemical attributes.” For example, a person of ordinary skill in the art would have appreciated that a  $^{35}\text{Cl}^-$  ion has the same **spatial structure** as a  $^{37}\text{Cl}^-$  ion, and that the two isotopes are chemically indistinguishable one from the other (the fact that isotopes of a same chemical element are chemically indistinguishable one from the other is established at page 5, lines 10 to 13 of the international publication). Accordingly, the person of ordinary skill in the art would not have been motivated to make the proposed modification, because Buryakov et al. teach that differences in spatial structure are required for separation, and isotopes of a same chemical element are known to have a same spatial structure within the meaning of the Buryakov et al. reference.

In fact, the **only** teaching that, despite being chemically indistinguishable one from the other, ions of two isotopes of a same chemical element may nevertheless be separated using FAIMS, is found in the instant application. For instance, Figure 12 of the application as originally filed shows a CV spectrum for the two isotopes of the chloride ion, namely  $^{35}\text{Cl}^-$  and  $^{37}\text{Cl}^-$ . The CV spectrum shown at Figure 12 is representative of the type of experimental results that may now be obtained by a skilled person who is in possession of the knowledge that two isotopes of a same element can be separated using FAIMS, and under optimized experimental conditions. Even under such ideal conditions, the peak maximum for the  $^{37}\text{Cl}^-$  isotope appears as little more than a shoulder upon the larger  $^{35}\text{Cl}^-$  peak. Applicant submits that it is only with the benefit of impermissible hindsight based upon a reading the instant application that it might now appear to be obvious to separate two isotopes of a same chemical element using FAIMS, as is claimed at claim 21.

In view of the arguments presented above, Applicant respectfully submits that claim 21 is in allowable form. Favorable reconsideration is kindly requested.

Previously presented claim 30 has been amended in order to correct a minor clerical error. In particular, the labels h)-l), in sequential order, were inadvertently indicated. Applicant submits that this error is attributed to the “auto-number function” of the word processing software. In amended claim 30, h)-l) in sequential order are relabeled as a)-e), also in sequential order. No new matter has been added in the amendment.

Having regard to claim 30, the same arguments that are presented with reference to claim 21 apply *mutatis mutandis*. Accordingly, Applicant respectfully submits that claim 30 is in allowable form. Favorable reconsideration is kindly requested.

Claim 37 depends from believed allowable claim 30 and is also believed to be in allowable form. Favorable reconsideration is kindly requested.

Claims 22 and 31 depend from believed allowable claims 21 and 30, respectively, and are also believed to be in proper form for allowance. Favorable reconsideration is kindly requested.

Claims 24, 25, and 27 depend from believed allowable claim 21 and are also believed to be in proper form for allowance. Favorable reconsideration is kindly requested.

Claims 33 and 34 depend from believed allowable claim 30 and are also believed to be in proper form for allowance. Favorable reconsideration is kindly requested.

Claims 29 and 36 depend from believed allowable claims 21 and 30, respectively, and are also believed to be in proper form for allowance. Favorable reconsideration is kindly requested.

Claims 23, 26, 28, 32, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buryakov et al. ("A new method of separation of multi-atomic ions by mobility at atmospheric pressure using a high-frequency amplitude-asymmetric strong electric field", International Journal Mass Spectrometry and Ion Processes, 1999) in view of Hudgins et al. ("High resolution ion mobility for gas phase proteins: correlation between solution phase and gas phase conformations", Int. Journal Mass Spec. and Ion Processes, 1997).

Claims 23, 26, and 28 depend from believed allowable claim 21 and are also believed to be in proper form for allowance. Favorable reconsideration is kindly requested.

Claims 32 and 35 depend from believed allowable claim 30 and are also believed to be in proper form for allowance. Favorable reconsideration is kindly requested.

Applicant looks forward to receiving favourable reconsideration of the present application.

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Respectfully,



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